PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 August 1999 (03.08.99)	
International application No. PCT/CA98/00997	**Applicant's or agent's file reference** 338-104PCT
International filing date (day/month/year) 28 October 1998 (28.10.98)	**Priority date** (day/month/year) 28 October 1997 (28.10.97)
Applicant STEEVES, John, D. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

28 May 1999 (28.05.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Lazar Joseph Panakal
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and Administrative Instructions, Sections 402 and 409)

To:

MBM & CO.
Station B
P.O. Box 809
Ottawa, Ontario K1P 5P9
CANADA

Date of mailing (day/month/year) 15 February 1999 (15.02.99)	
Applicant's or agent's file reference 338-104PCT	**IMPORTANT NOTIFICATION**
International application No. PCT/CA98/00997	International filing date (day/month/year) 28 October 1998 (28.10.98)
Applicant STEEVES, John, D. et al	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. [X] **Correction of priority claim.** In accordance with the applicant's notice received on: 05 February 1999 (05.02.99), the following priority claim has been corrected to read as follows:

CA 16 October 1998 (16.10.98) 2,251,410

- [ ] even though the indication of the number of the earlier application is missing.
- [ ] even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

2. [ ] **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:

- [ ] even though the indication of the number of the earlier application is missing.
- [ ] even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

3. [ ] As a **result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:

4. [ ] **Priority claim considered not to have been made.**

- [ ] The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
- [ ] The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
- [ ] The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(IB).

5. [ ] In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim(s):

6. A copy of this notification has been sent to the receiving Office and

- [X] to the International Searching Authority (where the international search report has not yet been issued).
- [X] the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer S. Cruz
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

Form PCT/IB/318 (July 1998)

002478049

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 39/395 // (A61K 39/395, 38:16) (A61K 39/395, 38:18)

A1

(11) International Publication Number: **WO 99/21581**

(43) International Publication Date: 6 May 1999 (06.05.99)

(21) International Application Number: PCT/CA98/00997

(22) International Filing Date: 28 October 1998 (28.10.98)

(30) Priority Data:

2,219,683	28 October 1997 (28.10.97)	CA
2,251,410	16 October 1998 (16.10.98)	CA

(71)(72) Applicants and Inventors: STEEVES, John, D. [CA/CA]; Cord, Depts, Zoology, Anatomy & Surgery, 6270 University Boulevard, Vancouver, British Columbia V6T 1Z4 (CA). DYER, Jason, K. [CA/CA]; Cord, Depts, Zoology, Anatomy & Surgery, 6270 University Boulevard, Vancouver, British Columbia V6T 1Z4 (CA). KEIRSTEAD, Hans, S. [CA/GB]; MRC Cambridge Centre for Brain Repair, Robinson Way, Cambridge CB2 2PY (GB).

(74) Agent: MBM & CO.; Station B, P.O. Box 809, Ottawa, Ontario K1P 5P9 (CA).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: IMMUNOLOGICAL COMPOSITIONS AND METHODS OF USE TO TRANSIENTLY ALTER MAMMALIAN CENTRAL NERVOUS SYSTEM MYELIN TO PROMOTE NEURONAL REGENERATION

(57) Abstract

Novel compositions are described comprising the combined administration of serum complement proteins with complement–fixing antibodies. The antibodies specifically bind to one or more epitopes of myelin, and complement proteins. These compositions are useful for promoting regrowth, repair, and regeneration of neurons in the CNS of a mammalian subject. The compositions and method can be used following immediate or chronic injury.

INTERNATIONAL SEARCH REPORT

Inter ›nal Application No
PCT/CA 98/00997

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K39/395 //(A61K39/395,A61K38:16),(A61K39/395,A61K38:18)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KEIRSTEAD, HANS S. ET AL: "Axonal regeneration and physiological activity following transection and immunological disruption of myelin within the hatchling chick spinal cord" J. NEUROSCI. (1995), 15(10), 6963-74 CODEN: JNRSDS;ISSN: 0270-6474, XP002091204 cited in the application	3,5,7, 20,31, 32,35
Y	see abstract see page 6971 - page 6973	4,6

-/--

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 January 1999	16/02/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mennessier, T

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter ›nal Application No
PCT/CA 98/00997

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	DYER, J. K. (1) ET AL: "Immunohistochemical and ultrastructural studies of adult chick and mouse myelin after intraspinal injection of serum complement proteins and myelin specific antibodies." SOCIETY FOR NEUROSCIENCE ABSTRACTS, (1995) VOL. 21, NO. 1-3, PP. 313. MEETING INFO.: 25TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE SAN DIEGO, CALIFORNIA, USA NOVEMBER 11-16, 1995 ISSN: 0190-5295., XP002091205 see the whole document	1-35
P,X	DYER, JASON K. ET AL: "Regeneration of brainstem-spinal axons after lesion and immunological disruption of myelin in adult rat" EXP. NEUROL. (1998), 154(1), 12-22 CODEN: EXNEAC;ISSN: 0014-4886, XP002091206 see the whole document	1-35
P,Y	KEIRSTEAD, HANS S. ET AL: "Identification of post-mitotic oligodendrocytes incapable of remyelinatio within the demyelinated adult spinal cord." JOURNAL OF NEUROPATHOLOGY & EXPERIMENTAL NEUROLOGY, (NOV., 1997) VOL. 56, NO. 11, PP. 1191-1201. ISSN: 0022-3069., XP002091207 cited in the application see abstract see page 1191, right-hand column, last paragraph see page 1193, right-hand column, last paragraph see page 1194, left-hand column	1-35
P,Y	KEIRSTEAD, H. S. (1) ET AL: "A quantifiable model of axonal regeneration in the demyelinated adult rat spinal cord." EXPERIMENTAL NEUROLOGY, (JUNE, 1998) VOL. 151, NO. 2, PP. 303-313. ISSN: 0014-4886., XP002091208 see page 303, left-hand column	1-35

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
338-104PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA98/00997	28/10/1998	28/10/1997
International Patent Classification (IPC) or national classification and IPC A61K39/395		
Applicant STEEVES, John, D. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28/05/1999	12.01.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Mennessier, T Telephone No. +49 89 2399 8687

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA98/00997

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-52 as originally filed

Claims, No.:

1-35 with telefax of 23/11/1999

Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 20-34 (with respect to industrial applicability).

because:

☒ the said international application, or the said claims Nos. 20-34 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-35
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-35
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-19, 35
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

1). Preliminary comments

The following documents which are cited in the international search report is mentioned in this written opinion:

* D1: *The Journal of Neuroscience*, 15(10), October 1995, 6963-74

* D2: *Journal of Neuropathology and Experimental Neurology*, 56(11), November 1997, 1191-201

* D3: *Exp. Neurol.*, 154(1), 1998, 12-22

* D4: *Exp. Neurol.*, 151(2), 1998, 303-313

2). Comments with regard to item I

The page containing Table 1 filed without being numbered has been also taken into consideration when preparing the present report.

3). Comments with regard to item III

Claims 20-34 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

4). Comments with regard to item V

a) Novelty (Article 33(2) PCT)

It is considered that the claimed subject-matter as a whole is new, as being not disclosed in any of the cited prior art non-intermediate documents.

b) Inventive step (Article 33(3) PCT)

(i) It is further considered that a person skilled in the art would not be in a position to deduce from document D1 (which, while reporting on the axonal regeneration and physiological activity following trnasection and immunological disruption of myelin within the hatchling chick spinal cord, is considered to represent the most relevant state of the art), when taken alone or in combination with the other non-intermediate document cited in the international search report, that **immunological transient alteration** of myelin **in mammals** carried out using one or more complement-fixing antibodies which specifically bind to an epitope of myelin in combination with one or more complement proteins would result in axonal regeneration. Therefore, it can be acknowledged that the claimed subject-matter as a whole also involves an inventive step.

c) Industrial applicability

For the assessment of the present claims 20-34 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

d) Intermediate documents

If it would appear that the priority could not be validly claimed, documents D2, D3 and D4 should be taken into account when assessing whether the various claimed aspects of the invention are new and involve an inventive step.

5). Comments with regard to item VII

a) The subject-matter of claim 21 appears to be redundant over that of claim 20.

b) Claim 35, while generally referring to components necessary to work the method of claim 31, fails to specify the precise components the claimed kit should actually be comprised of.

We claim:

1. A two-part composition for promoting the transient demyelination of neurons when combined in situ, in vivo with an epitope on myelin, wherein the two parts are intended to be admixed with each other either, before administration, at the time or administration, or after administration to a mammal in need of such treatment, which comprises:
(a) one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin; and
(b) one or more complement proteins or fragments thereof;
wherein the binding of said antibodies to myelin causes transient disruption and/or transient demyelination of myelin.

2. The two-part composition as in claim 1, wherein the composition additionally comprises one or more growth factors.

3. A composition comprising therapeutically effective amounts of the following:
(a) one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin; and
(b) one or more complement proteins or fragments thereof;
wherein the binding of said antibodies to myelin causes transient disruption and/or transient demyelination of myelin.

4. A composition as in claim 3, wherein the composition additionally comprises one or more growth factors.

5. A solution-system for the formation of a transiently demyelinating complex on the myelin of a neuron, wherein the components can be delivered separately or together which comprises:
(a) one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin; and
(b) one or more complement proteins or fragments thereof;

wherein the binding of said antibodies to myelin causes transient disruption and/or transient demyelination of myelin.

6. A solution-system as in claim 5, wherein the solution-system additionally comprises one or more growth factors.

7. The composition according to claim 1, 3, or 5, wherein the antibodies are monoclonal and/or polyclonal.

8. The composition according to claim 1, wherein some of the antibodies are labeled.

9. The composition according to claim 1, wherein the antibodies are an immunoreactive fragment selected from the group consisting of Fv, Fab, Fab', or F(ab')2 fragments.

10. The composition according to claim 9, wherein the variable regions of the Fv fragment are linked by disulfide bonds or by a peptide linker.

11. The composition according to claim 1, wherein the epitope of myelin is a myelin sheath epitope selected from the list including galactocerebroside (GalC), O4, Myelin Oligodendrocyte Glycoprotein (MOG), Myelin Associated Glycoprotein (MAG), NOGO, NI220, NI-35/250, or arretin.

12. The composition according to claim 1, wherein the complement proteins or fragments thereof include the C3 component or a fragment, variant, analog, or chemical derivative thereof.

13. The composition according to claim 1, wherein the complement proteins or fragments thereof are derived from species different from that species to which it is administered.

14. The composition according to claim 1, wherein the complement proteins or fragments thereof are a physically distinct component from the antibody component.

15. The composition according to claim 1, wherein the complement proteins or fragments thereof are covalently or noncovalently attached directly to the antibody component, such that binding of the antibody to the surface of the myelin triggers the endogenous immune system attack.

16. The composition according to claim 1, further comprising growth factors and neurotrophic factors.

17. The composition according to claim 16, wherein the neurotrophin is NT-3.

18. The composition according to claim 16, wherein the neurotrophin is FGF-1.

19. The pharmaceutical composition according to any of claim 1, further comprising a physiologically acceptable carrier.

20. A use of a composition, comprising therapeutically effective amounts of the following:
(a) one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin; and
(b) one or more complement proteins or fragments thereof;
wherein the binding of said antibodies to myelin causes transient disruption and/or transient demyelination of myelin, to promote neuron repair and/or regeneration in a subject by the disruption and/or demyelination of myelin.

21. The use according to claim 20, wherein the subject is mammalian.

22. The use according to claim 21, wherein the subject is human.

23. The use according to claim 22, wherein the subject is requiring neuron repair and/or regeneration due to neuron dysfunction.

24. The use according to claim 23, wherein the neuron dysfunction is caused by injury or trauma to the CNS.

25. The use according to claim 23, wherein the injury is a spinal cord injury.

26. The use according to claim 23, wherein the neuron dysfunction is caused by disease.

27. The use according to claim 26, wherein the disease is selected from the group consisting of Alzheimer's disease and Parkinson's disease.

28. The use according to claim 22, wherein the condition is chronic.

29. A use of a composition, comprising therapeutically effective amounts of the following:
(a) one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin; and
(b) one or more complement proteins or fragments thereof;
wherein the binding of said antibodies to myelin causes transient disruption and/or transient demyelination of myelin, to generate an environment within the mammalian CNS that is permissive to growth of transplanted cells.

30. A use of one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin, and which are labeled, to enable the detection and monitoring of the use of any of the compositions in claim 8.

31. A method of promoting neuron repair and/or regeneration in a subject by the transient disruption and/or transient demyelination of myelin, comprising contacting said neuron with therapeutically effective amounts of the following:
(a) one or more complement-fixing antibodies or fragments thereof, which specifically bind to an epitope of myelin; and
(b) one or more complement proteins or fragments thereof;

wherein the binding of said antibodies to myelin causes disruption and/or demyelination of myelin.

32. The method of claim 31, wherein one or more growth factors are added in an appropriate sequence to promote regrowth or regeneration.

33. The method of claim 31, wherein the subject is mammalian.

34. The method of claim 33, wherein the subject is human.

35. A kit comprising the components necessary to work the method of claim 31.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
338-104PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 98/00997	28/10/1998	28/10/1997
Applicant		
STEEVES, John, D. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

   [ ] filed with the international application.

   [ ] furnished by the applicant separately from the international application.

      [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

   [ ] Transcribed by this Authority

4. With regard to the **title**,

   [ ] the text is approved as submitted by the applicant

   [X] the text has been established by this Authority to read as follows:

IMMUNOLOGICAL COMPOSITIONS AND METHODS OF USE TO TRANSIENTLY ALTER MAMMALIAN CENTRAL NERVOUS SYSTEM MYELIN TO PROMOTE NEURONAL REGENERATION

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 98/00997

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K39/395 //(A61K39/395,A61K38:16),(A61K39/395,A61K38:18)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KEIRSTEAD, HANS S. ET AL: "Axonal regeneration and physiological activity following transection and immunological disruption of myelin within the hatchling chick spinal cord" J. NEUROSCI. (1995), 15(10), 6963-74 CODEN: JNRSDS;ISSN: 0270-6474, XP002091204 cited in the application	3,5,7, 20,31, 32,35
Y	see abstract see page 6971 - page 6973	4,6

-/--

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 January 1999	16/02/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mennessier, T

1

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	DYER, J. K. (1) ET AL: "Immunohistochemical and ultrastructural studies of adult chick and mouse myelin after intraspinal injection of serum complement proteins and myelin specific antibodies." SOCIETY FOR NEUROSCIENCE ABSTRACTS, (1995) VOL. 21, NO. 1-3, PP. 313. MEETING INFO.: 25TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE SAN DIEGO, CALIFORNIA, USA NOVEMBER 11-16, 1995 ISSN: 0190-5295., XP002091205 see the whole document	1-35
P,X	DYER, JASON K. ET AL: "Regeneration of brainstem-spinal axons after lesion and immunological disruption of myelin in adult rat" EXP. NEUROL. (1998), 154(1), 12-22 CODEN: EXNEAC;ISSN: 0014-4886, XP002091206 see the whole document	1-35
P,Y	KEIRSTEAD, HANS S. ET AL: "Identification of post-mitotic oligodendrocytes incapable of remyelinatio within the demyelinated adult spinal cord." JOURNAL OF NEUROPATHOLOGY & EXPERIMENTAL NEUROLOGY, (NOV., 1997) VOL. 56, NO. 11, PP. 1191-1201. ISSN: 0022-3069., XP002091207 cited in the application see abstract see page 1191, right-hand column, last paragraph see page 1193, right-hand column, last paragraph see page 1194, left-hand column	1-35
P,Y	KEIRSTEAD, H. S. (1) ET AL: "A quantifiable model of axonal regeneration in the demyelinated adult rat spinal cord." EXPERIMENTAL NEUROLOGY, (JUNE, 1998) VOL. 151, NO. 2, PP. 303-313. ISSN: 0014-4886., XP002091208 see page 303, left-hand column	1-35

1